REMARKS

With entry of the current amendment, claims 1, 11, and 32 have been amended.

Claims 5, 6, 15, 18-21, 28, and 33-49 have been previously cancelled. Claims 1-4, 1-10-14, 16, 17, 22-27, and 29-32 are thus currently pending.

The amendments to the claims add no new matter and are supported throughout the application as filed.

For convenience, the Examiner's rejections will be addressed in the order presented in the Office Action mailed August 20, 2003.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 11, 13, 14, and 17 are rejected as allegedly lacking adequate written description. It appears that the rejection relates only to the recitation of an immunoconjugate comprising a sequence encoding for a toxin peptide and "an antibody that binds to an RFB4 disulfide-stabilized Fv (dsFv)", which was found in the previous version of the claims. Amended claim 11 now recites that the immunoconjugate comprises a sequence encoding for a toxin peptide and an RFB disulfide-stabilized FV (dsFV). Applicants believe that this amendment fully addresses the rejection and therefore respectfully request its withdrawal.

Rejection under 35 USC § 103

The rejection alleges that claim 1-4, 7-11, 13, 14, 16, 17, 22-26, and 29-32 are unpatentable over the references cited in the previous Office Action and further in view of Hutson *et al.*, Robinson *et al.*, Cabilly *et al.*, and Boss *et al.* Applicants disagree for reasons of record. In short, the nucleic acid sequences of the RFB4 V_H and V_L are unobvious based on the current case law. The methods disclosed in the newly cited art are general methods for determining sequences of variable chain regions. There is no evidence that the prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention (*In re Deuel*, 34 USPQ2d, 1210 (Fed Circ. 1995)).

Furthermore, as Applicants have previously noted, the specification teaches that recombinant RFB4dsFv-PE38 has a binding affinity that is essentially equivalent to the binding affinity of the unconjugated RFB4 IgG (*see, e.g.*, page 41, lines 7-9). The retention of binding affinity that is equivalent to parent IgG cannot be predicted for a specific recombinant antibody. Reiter *et al.* (*Nature Biotechnology*) show that affinity that equals the IgG is seen only in a minority of cases. In response, the Examiner argues that Reiter *et al.* (*Biochemistry*) disclose that an scFv can retain the specificity and affinity of IgG, and that "dsFv's have at least the same binding properties as scFv's and in some cases they may be better". He therefore concludes that it would have been obvious that the claimed RFB4 dsFv's would have these properties. First, just because an scFv can retain the specificity and affinity of IgG and dsFv's can have the same or better binding properties that scFv's, it does not mean that this is a likely property.

Second, RFB4 variable regions have superior expression characteristics. As evidenced by the publication provided in Applicants' previous response (Krietman and Pastan, seminars in *Cancer Biology*), the art demonstrates that one of skill in the art cannot reasonably predict that a particular anti-CD22 scFv or dsFv construct will be expressed well and exhibit significant antitumor activity. The Examiner argues that this is only one example of a poorly expressing antibody where the dsFv had low activity. However, Applicants submit that this example is the closest art to the current claimed compositions, as the LL2 antibody binds to CD22, and is highly relevant.

In order to expedite prosecution, Applicants are preparing a Declaration under 37 C.F.R. § 1.132 by Dr. David FitzGerald that provides further evidence of both the surprising binding properties and cytotoxicity of the claimed immunoconjugates, and the superior expression characteristics of RFB4.

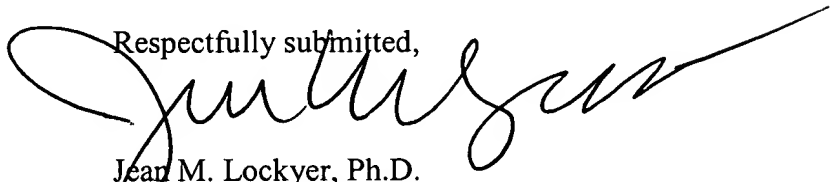
In view of the unexpected properties of the recombinant RFB4 immunotoxins, the claimed compositions are unobvious over the cited art. Applicants therefore respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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